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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,292	07/03/2001	Michele Amouyal	1231-01	2241

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EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 01/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,292	AMOUYAL, MICHELE	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-14,16-18,20-23 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14,16-18,20-23 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 3, 2006, has been entered.

Status of Application, Amendments, and/or Claims

2. Amendments of January 3, 2006, have been received and entered in full. Claims 11-14, 16-18, 20-23 and 28 are pending and under examination. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Interpretation

3. Claim 11 is amended to include the limitation "wherein said DNA compaction agent is present at a concentration sufficient to allow the DNA insert to remain flexible." This is read as any concentration that will permit the ligation reaction to occur. This could also read on specific concentrations necessary to permit unusual ligation reactions intended by applicant and not specified in the claim, therefore rejections are made under both 102 and 103.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-14, 16-18, 22, 23 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hodgson et al. (USPN 6,410,220 B1 06/25/2002).

Hodgson et al. teach (claims 11 and 28) a method for preparing circularized recombinant nucleic acids from a vector and an insert by ligating a DNA insert and a DNA vector in the presence of a DNA compaction agent selected from the group consisting of histone proteins, histone protein derivatives, viral envelope proteins, bacterial chromoid proteins, non-histone chromosomal proteins, HMGs derivatives of said proteins, and mixtures of said proteins and protein derivatives and selecting said circularized recombinant nucleic acid (see whole document, especially col. 23 lines 17-27). With regard to claims 12 and 27, they teach the circularized recombinant nucleic acid as greater than 5 and 10 kb (see col. 23 lines 22-24). With regard to claim 13, they teach the selection steps of transferring the circularized recombinant nucleic acid into a cellular medium, cloning nucleic acid, and testing for the presence of the insert in the circularized recombinant nucleic acid (see col. 23 lines 22-27). With regard to claim 14, they teach the DNA compaction agent is selected from the group consisting of a protein, a mixture of proteins and protein derivatives exhibiting the properties of the DNA compaction agent (see col. 23 lines 49-51). With regard to claims 16, 17, 18, they teach adding a ligase to a ligation medium containing the DNA in solution in ligation buffer or adding the compaction agent to the ligation medium prior to the addition of ligase or adding the ligase and the compaction agent simultaneously (see col. 23 line 52). With regard to claim 22, they teach the ligation medium comprising a stabilizing agent that prevents denaturation, aggregation, and absorption of the DNA compaction agent (see col. 23 line 52). With regard to claim 23, they teach histone proteins (see col. 23 line 51).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hodgson et al. (USPN 6,410,220 B1 06/25/2002) in view of Nagaki et al. (*BBRC* 246:137-141, 1998).

The teachings of Hodgson et al. are described previously.

Hodgson et al. do not teach a specific amount of HMG to use in the ligation reaction.

Nagaki et al. do teach using a range of 0.5 μg to 2.0 μg of HMG in the ligation reaction (see whole document, especially Fig. 2, page 139).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Nagaki's method of using a range of HMG concentrations with Hodgson's method of ligating insert and vector DNA in order to determine the amount of protein needed for the reaction. Nagaki et al. state that HMG1 and HMG2 stimulate cohesive-end and blunt-end ligations with DNA ligase (see col. 2 2nd paragraph pp 137-138). It would have been prima facie obvious to apply Nagaki's range of HMG concentrations with Hodgson's method for ligating insert and vector DNA to achieve the expected advantage of achieving optimal ligation activity with a given amount of DNA and HMG.

Response to Arguments

5. Applicant's arguments filed May 2, 2005, have been fully considered and are not found persuasive.

Applicant reiterates the argument that Hodgson teaches adding a DNA condensing agent after ligation.

This is not persuasive because Hodgson at col. 23 lines 49-52 states, "Another method is to add a DNA condensing reagent (dendrimers, polycations [such as polyethyleneamine] histones or liposomes) directly to the DNA ligation reaction." It is clear that the condensing agent is added directly to the ligation reaction. Typically a ligation reaction contains a vector, insert, ligase, buffer and in this instance a condensing agent. Hodgson does not disclose that the ligation reaction is completed prior to the addition of condensing reagent. Applicant argues that Hodgson teaches addition of condensing agent once the DNA segments have been joined. Applicants further argue Hodgson teach away from the present invention by teaching the addition of condensing agent once the DNA segments have joined and additionally teaching the addition of condensing reagent to the ligation reaction and then moving the DNA by pipette after it has been condensed. This is not persuasive because MPEP 2123 states, "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed...." In re Fulton, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004)." While Hodgson discloses the aforementioned teachings, Hodgson also disclosed adding the DNA condensing reagent directly to the DNA ligation reaction. Applicant additionally argues amended claims 11 and 28 recite the compaction agent is present at a concentration sufficient to allow the DNA insert to retain its flexibility and Hodgson's compaction agent is added in order to protect the DNA from shearing as shearing occurs when DNA is free in solution. This is not persuasive because DNA condensed on a histone protein is not rigid there is no evidence the DNA insert does not retain flexibility. The 102 (b) rejections over Hodgson are maintained.

With respect to the 103 (a) rejection, Applicant argues the instant invention is a DNA insert with enough flexibility to facilitate the construction of a large circularized recombinant nucleic acid molecules, and that Hodgson does not teach or suggest the use of a DNA compacting agent to provide flexibility.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues the deficiencies of Hodgson, however, these deficiencies are addressed by Nagaki. Nagaki teaches using a condensing agent, specifically histone proteins, during the ligation reaction. Nagaki further teaches histone proteins bind DNA in a sequence-non-specific manner and **bend** the DNA (see p. 137 col. 2, paragraph 2 sentence 3). The bending of the DNA connotes flexibility. Further, since condensing agent is added to the reaction and Hodgson does not indicate previously stopping the reaction, the reaction will reasonably continue. Therefore even if the condensing reagent was added after the reaction was set up the ligation is occurring in the presence of condensing reagent. Additionally, Nagaki et al. clearly disclose a ligation reaction in the presence of condensing reagent (see p. 139 Figure 2 and legend). Further Nagaki state, "Our present results demonstrate that both intra-molecular and inter-molecular ligations of the linearized PUCI 19 DNA (3.16 kbp) with DNA ligase IV were enhanced by HMGI and 2 (see p. 140 1st sentence under Discussion)." The 103 (a) rejections are therefore maintained.

Summary

6. No claims were allowable.

Correspondence

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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